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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/027,505	12/20/2001	Percy Carter	PH-7268	2093

23914 7590 01/13/2005

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EXAMINER	
RAO, DEEPAK R	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/027,505	CARTER ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-15,18-26,28-33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,11,12,15 and 19* is/are rejected.

7)☒ Claim(s) *2,4-10,13,14,18,20-26,28-33 and 35* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10122004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on October 12, 2004.

Claims 1-2, 4-15, 18-26, 28-33 and 35 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of rheumatoid arthritis, osteoarthritis, fever, and asthma, does not reasonably provide enablement for a method for modulation of chemokine or chemokine receptor activity; a method for treating autoimmune diseases generally; HIV-infection; cardiovascular effects, etc. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments and the cited references have been fully considered but they were not deemed to be persuasive. Applicant argues that 'the specification provides a description of the connection between MCP-1/CCR-2 and several diseases'. Applicant further provides some of the references cited in the specification in support of the arguments. However, no evidence

has been seen in the state of the art which establishes the single class of therapeutic agents as being effective against diverse generic diseases recited in the instant claims namely autoimmune diseases, cardiovascular effects, HIV infection, inflammatory bowel disease, etc. All of these diseases have diverse mechanisms and/or modes of action and effect different organs or body parts. There is no single therapeutic approach against all these diseases recognized in the state of the art. The references submitted by applicant also do not provide any supporting evidence for MCP-1/CCR-2 antagonists to be generally effective against all types of autoimmune diseases, cardiovascular effects or HIV infection. See the conclusive remarks in Fife et al., "Our data demonstrate an important role for specific chemokine receptor expression and in vivo cellular recruitment during the EAE pathogenesis and open the possibility of using **CCR-2 receptor antagonists for tissue specific autoimmune disease therapy**" (page 904). The state of the art reference only provides nexus between CCR-2 receptor antagonists and tissue specific autoimmune disease therapy. Other references also highlight the therapeutic ability of MCP-1/CCR-2 antagonists for specific diseases, see below:

Izikson et al.:"we de monstrate that **CCR2 is required for the pathogenesis of an organ-specific** T cell and macrophage-mediated inflammatory disease, **EAE, a model of MS** (i.e., multiple sclerosis)" (page 1079).

Tesch et al.: "to achieve more complete protection from autoimmune diseases in the MRL-Fas^{lpr} strain, **we will have to identify additional therapeutic targets**" (page 1822).

Reinecker et al.: "Our data suggests that MCP-1 may play a significant role in UC (ulcerative colitis) and CD (Crohn's Disease)" a nd "**Future investigations** of the role of

chemotactic cytokines in the upregulation of intestinal inflammation **may provide new understanding of the immunophysiology of IBD** as well as the basis for novel therapeutic strategies" (page 48).

Connor et al.: "Two additi onal -chemokine receptors CCR3 and CCR2b have also been shown to function as coreceptors for some, **but not all**, primary strains of HIV-1" (page 621) and "**Furth er studies will be necessary** to discriminate between these possibilities and delineate the pathogenic mechanisms associated with $CD4^+$ T cell depletion in vivo and the role of HIV-1 coreceptor use in this process" (page 626).

Smith et al.: "chemokine receptors C CR2 and CCR3 also have been implicated with HIV-1 coreceptors **on certain cell types**" (page 959).

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the **entire scope** of the pharmaceutical therapeutic activity of the instant claim. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). For all the above reasons, the rejection is maintained.

2. Claims 1, 11, 12 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Antoku et al., EP 443862, for the reasons provided in the previous office action which are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that the reference compounds are disclosed to have NMDA

receptor antagonist activity and does not teach or fairly suggest to modify the disclosed compounds in order to make compounds that are MCP-1/CCR-2 receptor antagonists. However, the prior art need not disclose the newly discovered property in order for there to be a *prima facie* case of obviousness. In fact, similar properties may normally be presumed when compounds are very close in structure. Also note, there is no requirement that the prior art must suggest that the claimed compound will have the same or similar utility as that discovered by applicant in order to support a legal conclusion of obviousness. *In re Dillon*, 919 F.2d 688, 696, 16 U.S.P.Q.2d 1897, 1904 (Fed. Cir. 1991). If the prior art compound does in fact possess a particular benefit, even though the benefit is not recognized in the prior art, applicant's recognition of the benefit is not in itself sufficient to distinguish the claimed compounds from the prior art. The reference teaches that the compounds have pharmaceutical therapeutic activity, which is sufficient to one of ordinary skill to make the claimed compounds because similar properties are normally presumed when compounds are very close in structure. There is nothing on the record to show that the reference compounds do not possess the activity of the instant compounds. Applicants must prove that their compounds possess a property that the prior art compounds do not possess. The discovery of additional use not disclosed in the reference does not make otherwise obvious compounds unobvious. See *In re Best*, 195 USPQ 430 (CCPA 1977). The PTO can require an applicant to prove that the relevant prior art products do not necessarily or inherently possess characteristics of the claimed product. As there is no comparative data on record clearly establishing that the properties of the instant compounds are "unexpected" when compared to those of the reference compounds, the rejection is maintained.

Allowable Subject Matter

Claims 2, 4-10, 13-14, 18, 20-26, 28-33 and 35 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Receipt is acknowledged of the Information Disclosure Statement filed on October 12, 2004 and a copy is enclosed herewith.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

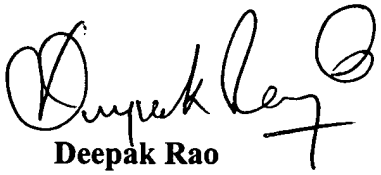
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Deepak Rao
Primary Examiner
Art Unit 1624

January 12, 2005